ABSTRACT OF THE DISCLOSURE

[0220] The present invention provides an isolated, functionally-active protein that catalyzes cleavage of a gamma-secretase substrate. The functional activity of the isolated protein suggests that the isolated protein includes gamma-secretase. In one embodiment, the isolated gamma-secretase protein is associated with PS1. The present invention also relates to homogeneous methods for monitoring cleavage of β-amyloid precursor protein (βAPP) by gamma-secretase, wherein the steps of of isolating and retrieving cleavage products have been eliminated. Cleavage can be detected by binding a pair of fluorescent adducts to the gamma-cleaved βAPP fragment. Preferably, a first fluorescent adduct binds to the carboxy-terminal end of the gamma-cleaved βAPP fragment, with substantially no cross-reactivity to uncleaved βAPP or to other types of gamma-cleaved βAPP fragments, while a second fluorescent adduct binds to a portion within the amino-terminal region on the gamma-cleaved βAPP fragment. Detection of binding to the gamma-cleaved βAPP fragment is determined by monitoring the fluorescent energy transfer between the adducts.